Organs-on-chip: towards therapies for cardiovascular disease using human stem cells

Helden, R.W.J. van

CURRICULUM VITAE

Ruben Willem Joseph van Helden was born on march 6th 1990 in 's Gravenhagen in The Netherlands. He commenced his Bachelor's degree in Biomedical Sciences at Leiden University in 2010. He completed his bachelor's with a four-month internship in the Leiden University Medical Center (LUMC) at the Department of Parasitology under the supervision of prof.dr. Maria Yazdanbakhsh with the aim of studying the relationship between Schistosoma, the development of allergies, and serum immunoglobulins in a cohort of children from Ghana.

After his bachelor's, Ruben pursued a Research Master's in Biomedical Siences at the LUMC where he started to develop his interest in stem cell research. His first foray into this was a five-month research internship at LUMC in the Department of Nephrology in the lab of prof.dr. Eelco de Koning, where he investigated the pancreatic duct niche for a potential primary stem cell candidate. Subsequently, he continued to work as a research assistant at the Department of Nephrology for prof.dr.Ton Rabelink, analysing electron microscopy images of the glomerulus. During this period, he was also a member of the Biomedical Sciences yearly student representation committee and a student member of the Education Committee for the study program. Finally, he completed his master's with an eight-month internship under prof.dr. Kevin Eggan at the Harvard Department of Stem Cell and Regenerative Biology. Here, he investigated the role of *SOD1* mutation in the development of amyotrophic lateral sclerosis in human induced pluripotent stem cell (hiPSC)-derived motor neurons and the development of the action-potential initiation segment in these motor neurons. For this work, he was awarded scholarships from the Dutch ALS fund, the Leiden University International Study Fund, the Minerva Scholarship Foundation, and the Jo Keur Fund. His research proposal was nominated for the Janne Fruin-help prize and his master's thesis was nominated for the LIFS prize.

Ruben's interest in stem cell research flourished, and he started his PhD in 2016 under the supervision of prof.dr. Christine Mummery, dr. Milena Bellin and dr. Valeria Orlova in the Department of Anatomy and Embryology at the LUMC. During this period he studied the effects of mutations leading to mitochondrial infantile cardiomyopathy in hiPSC-derived cardiomyocytes, specialised in metabolic assays, and developed an interest in developing a more complex *in vitro* model and the organ-on-chip field. During this period, he co-started and was a member of the early researcher committee for both the local and international reNEW consortium, funded by Novo Nordisk. He was additionally awarded a travel grant and presentation award at the Dutch-German cardiovascular meeting. In 2022 he continued his work as a post-doc and lab manager under prof.dr. Christine Mummery for the reNEW consortium.

Since 2023 Ruben has moved to Vienna to work as a senior scientist at the start-up company HeartBeat.bio working toward the development of a high-throughput 3D screening platform for heart diseases using self-organizing human cardiac organoids.

LIST OF PUBLICATIONS

1. Arslan U, Brescia M, Meraviglia V, Nahon DM, **Helden RWJ van**, Stein JM, Hil FE van den, Meer BJ van, Cuenca MV, Mummery CL, *et al* (2023) Vascularized hiPSC-derived 3D cardiac microtissue on chip. *Stem Cell Rep* 18: 1394–1404
2. Brandao KO, **van Helden RWJ**, van den Brink L, Blanch-Asensio A, Mol MPH, Kuipers T, Mei H, Mummery CL & Davis RP Investigating the molecular consequences of KCNH2 compound mutations in hiPSC-derived cardiomyocytes. Proefschrift (2023) Karina O. Brandão chapter 6
3. Campostrini G, Meraviglia V, Giacomelli E, **van Helden RWJ**, Yiangou L, Davis RP, Bellin M, Orlova VV & Mummery CL (2021) Generation, functional analysis and applications of isogenic three-dimensional self-aggregating cardiac microtissues from human pluripotent stem cells. *Nat Protoc* 16: 2213–2256
4. Giacomelli E, Meraviglia V, Campostrini G, Cochrane A, Cao X, **van Helden RWJ**, Krotenberg Garcia A, Mircea M, Kostidis S, Davis RP, *et al* (2020) Human-iPSC-Derived Cardiac Stromal Cells Enhance Maturation in 3D Cardiac Microtissues and Reveal Non-cardiomyocyte Contributions to Heart Disease. *Cell Stem Cell* 26: 862-879.e11
5. **van Helden RWJ**, Fuchs S, Wiendels M, de Graaf MNS, Orlova VV, Mummery CL, van Meer BJ & Mayr T (2022) On-chip analysis of glycolysis and mitochondrial respiration in human induced pluripotent stem cells. *Mater Today Bio* 17: 100475
6. **van Helden RWJ**, Birket MJ, Freund C, Arendzen CH, Mikkers HM, Orlova V, de Coo RI, Mummery CL & Bellin M (2021) Generation of three human induced pluripotent stem cell lines, LUMCi024-A, LUMCi025-A, and LUMCi026-A, from two patients with combined oxidative phosphorylation deficiency 8 and a related control. *Stem Cell Res* 53: 102374
7. **van Helden RWJ**, de Korte T, Kostidis S, Mei H, Slieker RC, Knoops K, Mulder AA, Davis RP, Giera M, de Coo RI, *et al* Disrupted energetics and contraction in cardiomyocytes with infantile mitochondrial cardiomyopathy. *Manuscript submitted to Embo Molecular Medicine*
8. de Korte T, **van Helden RWJ**, François L, Meraviglia V, Mol MPH, Yiangou L, Bellin M, Braam SR, Mummery CL & Davis RP Industrialization of 3D hiPSC-cardiac (disease) microtissues for high-throughput functional screening in drug discovery. *Manuscript in preparation*
9. del valle JS, **van Helden RWJ**, Moustakas I, Wei F, Asseler JD, Metzemaekers J, Gonneke PSK, Mummery CL, Westerlaken LAJ, van Mello N, *et al* Ex vivo removal of pro-fibrotic collagen and rescue of metabolic function in human ovarian fibrosis. *Manuscript submitted to iScience*
10. Weener HJ, van Haaps TF, **van Helden RWJ**, Albers HJ, Haverkate R, Middelkamp H, Ridderikhof ML, van Mens TE, van den Berg A, Mummery CL, *et al* Blood-perfused Vessels-on-Chips stimulated with patient plasma recapitulate endothelial activation and microthrombosis in COVID-19. *Manuscript in preparation for Nature Microphysiological Systems*

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